

Translation

## PATENT COOPERATION TREATY

# PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>03/058 LTSBOE</b>	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. <b>PCT/EP2004/007770</b>	International filing date (day/month/year) <b>14.07.2004</b>	Priority date (day/month/year) <b>23.07.2003</b>
International Patent Classification (IPC) or national classification and IPC <b>A61K31/428, A61K9/70</b>		
Applicant <b>LTS LOHMANN THERAPIE-SYSTEME AG</b>		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <b>9</b> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (<i>sent to the applicant and to the International Bureau</i>) a total of <b>2</b> sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> <p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasons statement under Article 35(2), with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/EP2004/007770

## Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
 

This report is based on translations from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
 
  - international search (Rule 12.3 and 23.1(b))
  - publication of the international application (Rule 12.4)
  - international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):
 

the international application as originally filed/furnished  
 the description:  
 pages 1-10 as originally filed/furnished  
 pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_  
 pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

the claims:  
 nos. \_\_\_\_\_ as originally filed/furnished  
 nos.\* \_\_\_\_\_ as amended (together with any statement) under Article 19  
 nos.\* 1-30 received by this Authority on 23.05.2005 with letter of 23.05.2005  
 nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

the drawings:  
 sheets \_\_\_\_\_ as originally filed/furnished  
 sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_  
 sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3.  The amendments have resulted in the cancellation of:
 

the description, pages \_\_\_\_\_  
 the claims, nos. \_\_\_\_\_  
 the drawings, sheets/figs \_\_\_\_\_  
 the sequence listing (*specify*): \_\_\_\_\_  
 any table(s) related to sequence listing (*specify*): \_\_\_\_\_
4.  This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 

the description, pages \_\_\_\_\_  
 the claims, nos. \_\_\_\_\_  
 the drawings, sheets/figs \_\_\_\_\_  
 the sequence listing (*specify*): \_\_\_\_\_  
 any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/EP2004/007770

## Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

the entire international application

claims Nos. 19-22, 27-30

because:

the said international application, or the said claims Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international preliminary examination (*specify*):

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for said claims Nos. 19-22, 27-30

the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

has not been furnished

does not comply with the standard

the computer readable form

has not been furnished

does not comply with the standard

the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

See Supplemental Box for further details.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/EP2004/007770Box No. V      Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	16, 21	YES
	Claims	1-15, 17-20, 22-30	NO
Inventive step (IS)	Claims		YES
	Claims	1-30	NO
Industrial applicability (IA)	Claims	1-18, 23-26	YES
	Claims		NO

## 2. Citations and explanations (Rule 70.7)

See Supplemental Box.

**Supplemental Box**

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

*Continuation of Boxes III and V*

**BOX III****Non-establishment of opinion with regard to novelty,  
inventive step and industrial applicability**

**Claims 19 to 22 and 27 to 30** relate to subject matter which, in the opinion of this Authority, falls under **PCT Rule 67.1(iv)**. Consequently no expert opinion has been established regarding the industrial applicability of the subject matter of these claims (**PCT Article 34(4) (a) (i)**).

**BOX V****Reasoned statement with regard to novelty, inventive step  
and industrial applicability; citations and explanations  
supporting such statement**

This report refers to the following documents:

- D1:** EP 0 428 038 A (BOEHRINGER INGELHEIM), 22 Mai 1991  
(1991-05-22)
- D2:** WO 03/015779 A (HEXAL), 27 February 2003 (2003-02-27)
- D3:** WO 02/03969 A (HEXAL), 17 January 2002 (2002-01-17)
- D4:** WO 00/74661 A (NOVEN PHARMACEUTICALS), 14 December 2000  
(2000-12-14)
- D5:** WO 03/011291 A (HEXAL), 13 February 2003 (2003-02-13)
- D6:** WO 96/18395 A (UPJOHN), 20 June 1996 (1996-06-20)

## Supplemental Box

1. The PCT Contracting States do not have uniform criteria against which the industrial applicability of **claims 19 to 22 and 27 to 30** in the present application can be assessed. Patentability may depend on the wording of the claims. For example, the European Patent Office does not recognise the industrial applicability of claims to the medical use of a compound. It may, however, allow claims to the first medical use of a known compound or to the use of such a compound in the preparation of a drug for a new medical application.
2. The application fails to meet the requirements of PCT Article 33(1) because the subject matter of **claims 1, 3, 4, 7 to 15, 19, 20, 22 to 24, 26 to 28 and 30** is not novel (PCT Article 33(2)) over document D1.

**Document D1** describes a transdermal therapeutic system for treating **schizophrenia** and **parkinsonism**, consisting of a back layer, a peel-off protective film and **an active-principle-containing film reservoir**, exactly as in the present invention, **the active principle (Pramipexol or its (-) enantiomer)** being contained in **an emulsion polymerised polyacrylate polymer layer**. The polyacrylate polymer layer is of the type Eudragit NE 30 D (R) (**a mixture of carboxyl-group-free polymerised acrylic esters and methacrylic esters**). The system can **apply between 0.5 and 5 mg of the active principle per day with a flow rate of more than 10 micrograms/cm<sup>2</sup> h** (see D1, page 2, lines 40 to 50; also the claims, example 1 and figure I).

The subject matter of **claims 1 to 9, 14, 19, 22, 23**,

## Supplemental Box

**25 to 27, 29 and 30** lacks novelty (**PCT Article 33(1)** and **33(2)**) over document **D2**.

**Document D2** discloses (the references in parentheses are to D2) a transdermal therapeutic system for treating **parkinsonism**, consisting of a cover layer, a peel-off protective film and one (or more) **active-principle-containing matrix layer(s), the active principle (Pramipexol or salts or solvates thereof) being contained in an polyacrylate polymer layer**. The polyacrylate polymer layer can be of the type Durotak 2287 (R), exactly as in the present invention (see *D2, page 4, third paragraph to page 8, first paragraph; also the claims and examples*).

**In a similar way** the subject matter of **claims 1 to 9, 14, 17 to 19, 23 and 27** lacks novelty (**PCT Article 33(1)** and **33(2)**) over document **D3**.

**Document D3** discloses (the references in parentheses are to D3) a transdermal therapeutic system comprising a cover layer, a peel-off protective film and **one (or more) active-principle-containing self-adhesive matrix layer(s)**, in which **the active principle, which can be an antiparkinsonism agent such as Pramipexol, is contained in an polyacrylate polymer layer**. The polyacrylate polymer layer can be of the type **Durotak (R)**, exactly as in the present invention (see *D3, page 13, third paragraph; page 8, first paragraph to page 9, first paragraph; and the claims*). **The system can contain penetration promoters (such as silicon dioxide or alcohols such as 1,2-propane diol) or stabilisers.**

## Supplemental Box

In a similar way the subject matter of claims 1 to 9, 14, 17 to 19, 23 and 27 lacks novelty (PCT Article 33(1) and 33(2)) over document D4.

Document D4 discloses (the references in parentheses are to D4) a transdermal therapeutic system comprising an active-principle-containing self-adhesive matrix layer, in which the active principle, which can be an antiparkinsonism agent such as Pramipexol, is contained in an polyacrylate polymer layer. The polyacrylate polymer layer, which can be of the type Durotak (R), exactly as in the present invention, contains a polymerised hydroxyl-group-containing acrylic ester (see D4, page 18, first paragraph; and the claims and examples). The system can contain penetration promoters (such as alcohols or diols such as 1,2-propane diol) or stabilisers (such as esterified cellulose derivatives). The subject matter of claims 1 to 15, 17 to 20 and 22 to 30 therefore lacks novelty (PCT Article 33(1) and 33(2)).

3. The application fails to meet the requirements of PCT Article 33(1) because the subject matter of claims 1 to 30 does not involve an inventive step (PCT Article 33(3)).

Regarding the subject matter of claims 1 to 30, documents D1 to D4 appear to be of particular relevance in connection with the question of inventive step. They in fact solve the same problem, namely that of providing transdermal therapeutic systems comprising a back layer

## Supplemental Box

and an active-principle-containing polymer matrix, and containing **an antiparkinsonism agent such as Pramipexol (or its (-) enantiomer or salts or solvates thereof)**. The active-principle-containing polymer matrix is a **polyacrylate polymer layer created from a mixture of carboxyl-group-free and hydroxyl-group-containing polymerised acrylic esters and methacrylic esters**. These transdermal therapeutic systems are designed to have a particular daily release rate and flow rate.

Regarding the subject matter of **claims 16 and 21**, it seems to be normal to choose a specific concentration of the active principle and to use Pramipexol as a neuroprotective drug (the neuroprotective action of Pramipexol is well established; see document D6).

The present application therefore does not appear to meet the requirements of **PCT Article 33(1) and 33(3)** with respect to the aforementioned documents in so far as novelty is concerned.